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10/054,567	11/13/2001	Christel Schmelzer	1/1171	7734

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EXAMINER

JIANG, SHAOJIA A

ART UNIT	PAPER NUMBER
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1617

DATE MAILED: 08/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/054,567

Applicant(s)

SCHMELZER ET AL.

Examiner

Shaojia A. Jiang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 June 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 7-12, 15-21 and 28-46 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 7-12, 15-21 and 28-46 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>6/6/05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This Office Action is in response to Applicant's amendment and response filed on June 6, 2005 wherein the instant specification has been amended as to page 13 line 33-35 **not** page 12 line 32-33 as Applicant asserts in the amendment; claims 1-4, 7-12, 15-21, and 28-46 have been amended; claims 5-6, 13-14, and 22-27 are cancelled previously.

Currently, claims 1-4, 7-12, 15-21, and 28-46 are pending in this application.

Claims 1-4, 7-12, 15-21, and 28-46 are currently under examination on the merits.

Applicant's declaration of Alexander Walland (not inventor), submitted June 6, 2005 under 37 CFR 1.132, is acknowledged and will be further discussed below.

Applicant's amendment that amends the specification with respect to the objection for the incorporation of essential material in the specification at page 13, lines 34-35 by reference to a foreign application or patent, or to a publication, i.e., WO 97/12687, of record stated in the Office Action dated February 8, 2005 has been fully considered and is found persuasive. Therefore, this said objection is withdrawn.

Objection to the Specification

However, it is noted for the record that reference to a foreign application, i.e., WO 97/07607, also appears at page 11, last para.; WO 97/20590 appears at page 13, 1st and 6th para. of the specification herein.

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication, as pointed out above, is improper.

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Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

See also *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

Applicant's remarks filed June 6, 2005 with respect to the rejection of claim 43, made under 35 U.S.C. 112, second paragraph, for indefinite recitation, "according to Figures 1a and 1b. " in claim 43 of record in the previous Office Action dated February 8, 2005, have been fully considered and found persuasive to remove the rejection, since the propriety of referencing figures in claims is provided for in MPEP 2173.05(s), "Reference to Figures or Tables". In this case, "there is no practical way to defined the invention in words, it is more concise to incorporate by reference than duplicating the drawing as depicted in Figures 1a and 1b" as Applicant asserts, Therefore, the said rejection is withdrawn.

The following is the new obviousness-type double patenting rejection(s).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

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unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 7-12, 15-21, and 28-46 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,630,466.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent is drawn to the same composition or method of treating a respiratory disease comprising the same or substantially same agents or ingredients: 1) a salt of tiotropium or tiotropium bromide and 2) salmeterol or its pharmaceutically acceptable salt, as instantly claimed.

Thus, the instant Claims 1-4, 7-12, 15-21, and 28-46 is seen to be anticipated by the claims 1-10 of U.S. Patent No. 6,630,466.

Claims 1-4, 7-12, 15-21, and 28-46 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 10-14 of U.S. Patent No. 6,680,345.

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Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent is drawn to the same composition or method of treating a respiratory disease such as asthma or COPD, comprising the same or substantially same agents or ingredients: 1) salmeterol or its pharmaceutically acceptable salt and 2) a salt of tiotropium or tiotropium bromide, as instantly claimed.

Thus, the instant Claims 1-4, 7-12, 15-21, and 28-46 is seen to be anticipated by the claims 1-10 of U.S. Patent No. 6,630,466.

Claims 1-4, 7-12, 15-21, and 28-46 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4-23 of U.S. Patent No. 6,919,325.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent is drawn to the same composition or method of treating a respiratory disease such as asthma or COPD, comprising the same or substantially same agents or ingredients: 1) a salt of tiotropium or tiotropium bromide and 2) salmeterol or its pharmaceutically acceptable salt, as instantly claimed. The patent 6,919,325 also claims the ratio of 1) to 2) within the instantly claimed range (see claims 9-10 of the patent).

Thus, the instant Claims 1-4, 7-12, 15-21, and 28-46 is seen to be anticipated by the claims 1, 4-23 of U.S. Patent No. 6,919,325.

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Claims 1-4, 7-12, 15-21, and 28-42 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of copending Application No. 10/736,264, of record stated in the Office Action dated February 8, 2005.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending Application is drawn to a composition comprising tiotropium and salmeterol salts as the instantly claimed.

Thus, the instant claims 1-4, 7-12, 15-21, and 28-42 are seen to be anticipated by the claims 1-20 of copending Application No. 10/736,264.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-4, 7-12, 15-21, and 28-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over FREUND et al. (WO 97/01329 in German, equivalent to US 6,491,897, PTO-892) in view of Hochrainer et al and Wolf et al.(of record), essentially for same reasons of record stated in the Office Action dated February 8, 2005.

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Freund et al. discloses a propellant free pharmaceutical composition comprising the active agents or combinations of active agents including tiotropium bromide and salmeterol (see 6,491,897, the title, abstract, col.1 line 66 to col. 2 line 15, especially col.2 line 5, 8, 15), which is in a form suitable for inhalation administration, i.e. use in nebulizers (see abstract and col.2 line 1). The pharmaceutical composition of Freund et al. comprises acids such as hydrochloride acid, sulphuric acid, phosphoric acid (see col.2 line 60-64) which form a pharmaceutically acceptable salts with the active agents, and also comprises adjuvant (see col. 5 line 14-15), and water and ethanol (see col.1 line 40-48) wherein the pH of the solution is in the range of 2-7, especially 3-4 or 3.2-4.5 within the instantly claimed range (see col.2 line 66-67; claim 2-3), and cosolvent such as isopropyl alcohol, polypropylene glycol, glycol ether (see col.1 line 51-58), and flavoring and ascorbic acid and other adjuvants (see col.2 line 62-64). The propellant free pharmaceutical composition therein is useful in a method of treating obstructive lung diseases such as asthma (see col.1 line 11-15).

Freund et al. does not expressly exemplify the particular combination composition of tiotropium bromide and salmeterol. Freund et al. does not does not expressly disclose the effective amounts of tiotropium bromide and salmeterol in the composition herein to be administered. Freund et al. does not does not expressly disclose the compositions therein contained in single preparation or two separate preparations.

Hochrainer et al and Wolf et al teach the claimed tiotropium and salmeterol respectively as old and well known in combination with various pharmaceutical carriers

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and excipients in both a powder and liquid form useful for atomization. Hochrainer et al. teach tiotropium and other asthma, and COPD medicaments in combination with polyalcohols, (page 5), EDTA (page 5, line 26), benzalkonium chloride (page 5, line 66), vitamin C (page 4, line 58). These compositions are taught in the particle size range ((970) page 5, line 10-15), pH (4970) page 4, line 60-62) and encapsulation schema herein envisioned. These pharmaceutical formulations are taught as useful for treating COPD and asthma, viewed by the skilled artisan as indistinguishable from that use herein claimed.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the particular combination composition of tiotropium bromide and salmeterol, and to optimize the effective amounts of active agents in the composition herein to be administered, and to store the combination in a single or two separate containers.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the particular combination composition of tiotropium bromide and salmeterol, since the combinations of active agents including tiotropium bromide and salmeterol in a propellant free pharmaceutical composition is disclosed by Freund et al. Thus, any combinations of active agents including tiotropium bromide and salmeterol disclosed by Freund et al. would have had the reasonable expectation of success as used in a propellant free pharmaceutical composition for treating obstructive lung diseases such as asthma.

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Additionally, one of ordinary skill in the art would have been motivated to optimize the effective amounts of active ingredients in the composition because tiotropium and salmeterol respectively are old and well known to be used in treating COPD and asthma according to Hochrainer et al and Wolf et al. Thus, the optimization of the known amounts of the known active agents to be administered is considered well within the skill of artisan.

Moreover, one of ordinary skill in the art would have reasonably expected that combining tiotropium and salmeterol both known useful for the same purpose, i.e., treating COPD and asthma, would improve the therapeutic effects for treating the same diseases, and/or would produce additive therapeutic effects in treating the same.

It has been held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; idea of combining them flows logically from their having been individually taught in prior art. See *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980.

Further, the patient pack, e.g., a single or two separate containers, is all deemed obvious since they are all within the knowledge and conventional skills of pharmacologist to conveniently assist the user and prescriber for easy dispensary of the medication.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Response to Argument

Applicant's arguments and the declaration of Alexander Walland, under 37 CFR 1.132, filed June 6, 2005 with respect to this rejection made under 35 U.S.C. 103(a) of record in the previous Office Action February 8, 2005 have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art as further discussed below.

Applicant's argue that [t]he Examiner fails to provide a specific teaching in either Hochrainer or Wolf to the claimed combination" and there is no teaching, suggestion, or incentive in Hochrainer or Wolf to modify the singly specifically expemlified composition containing the combination claimed herein.

Applicant's arguments are not found persuasive. In this case, the primary reference cited herein, Freund et al. discloses a propellant free pharmaceutical composition comprising the active agents or combinations of active agents including tiotropium bromide and salmeterol, which is in a form suitable for inhalation administration, i.e. use in nebulizers (see abstract and col.2 line 1). The pharmaceutical composition of Freund et al. comprises acids such as hydrochloride acid, sulphuric acid, phosphoric acid which form a pharmaceutically acceptable salts with the active agents, and also comprises adjuvant (see col. 5 line 14-15), and water and ethanol (see col.1 line 40-48) wherein the pH of the solution is in the range of 2-7, especially 3-4 or 3.2-4.5 within the instantly claimed range, and cosolvent such as isopropyl alcohol, polypropylene glycol, glycol ether, and flavoring and ascorbic acid and other adjuvants.

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The propellant free pharmaceutical composition therein is useful in a method of treating obstructive lung diseases such as asthma, as instantly claimed.

Thus, any combinations of active agents including tiotropium bromide and salmeterol disclosed by Freund et al. would have had the reasonable expectation of success as used in a propellant free pharmaceutical composition for treating obstructive lung diseases such as asthma.

Therefore, the disclosure of Freund et al. has clearly provided the motivation to make the present invention, a propellant free pharmaceutical composition comprising tiotropium and salmeterol or their salts.

Moreover, Hochrainer et al and Wolf et al have been cited by the examiner primarily for its teaching that the claimed tiotropium and salmeterol respectively as old and well known in combination with various pharmaceutical carriers and excipients in both a powder and liquid form useful for atomization and in methods for treating asthma, and COPD.

Thus, the claimed invention is clearly obvious in view of the prior art.

Further, Applicant's declaration (of Alexander Walland) under 37 CFR 1.132, is insufficient to overcome the 103(a) rejection herein. The testing results in the declaration merely show that a single combination of tiotropium bromide in 3 µg and salmeterol hemisulfate in 6 µg or 12 µg. Note that unexpected results to rebut the prima facie case, the scope of the showing must be commensurate with the scope of the claims. *In re Coleman*, 205 USPQ 1172; *In re Greenfield*, 197 USPQ 227; *In re Lindener*, 173 USPQ 356; *In re Payne*, 203 USPQ 245. In the instant case, the

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evidence in the examples herein is also not commensurate in scope with the claimed invention and does not demonstrate criticality of a claimed range of the ingredients in the claimed composition, and in the claimed range of the ratio of tiotropium and salmeterol. See MPEP § 716.02(d).

Therefore, the evidence presented in Applicant's declaration herein is not seen to be clear and convincing in support the nonobviousness of the instant claimed invention over the prior art.

For the above stated reasons, said claims are properly rejected under 35 U.S.C. 103(a). Therefore, said rejection is adhered to.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



S. Anna Jiang, Ph.D.
Primary Examiner
Art Unit 1617
August 9, 2005